

This Page Is Inserted by IFW Operations  
and is not a part of the Official Record

## **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning documents *will not* correct images,  
please do not report the images to the  
Image Problem Mailbox.**

JCWSCS 07 JUL 2004

07/06/2004 14:46 FAX 1 415 398 3249

DORSEY &amp; WHITNEY LLP-SF

001



## FAX COVER SHEET

The information contained in this facsimile message, if a client of this firm is a named addressee, or the message is otherwise intended for a client, is presumptively legally privileged and confidential information. If you are not a named addressee, or if there is any reason to believe you may have received this message in error, (1) do not read the message below; (2) do not distribute or copy this facsimile; and (3) immediately call us collect at the number of the sender below.

DATE:	July 7, 2004	TOTAL # OF PAGES: (INCLUDING THIS COVER SHEET)	10
TO:	Office of Initial Patent Examination's Filing Receipt Corrections	FAX #:	703-746-9195
FIRM NAME:	U.S. Patent and Trademark Office	PHONE #:	
FROM:	Victoria Poulsen for Renee M. Kosslak	FAX #:	(415) 398-3249
PHONE #:	(415) 544-7036	EMAIL:	poulsen.victoria@dorsey.com

## COMMENTS:

Request for Corrected Filing Receipt with Supporting Memoranda enclosed for  
U.S. Patent Application Serial No. 10/820,465

ORIGINAL WILL BE SENT VIA: ☐ MAIL ☐ E-MAIL ☐ MESSENGER ☐ AIR COURIER ☒ WILL NOT BE SENT  
PLEASE CONTACT VICTORIA POULSEN AT (415) 544-7036 IF THIS TRANSMISSION IS INCOMPLETE OR CANNOT BE RECORDED

REFERENCE # 34100 470425-272

DORSEY & WHITNEY LLP · WWW.DORSEY.COM · T 415.781.1989 · F 415.3249  
FOUR EMBARCADERO CENTER · SUITE 3400 · SAN FRANCISCO, CALIFORNIA 94118  
USA CANADA EURO ASIA

PATENT

Attorney Docket No. 34099/US/2 (463077-00267)

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

Desjarlais et al.

Serial No. 10/820,465

Filed: March 31, 2004

For: ***April Variants and Methods  
for Rational Pegylation of  
Proteins***

Group Art No. 1646

Examiner: Not Assigned

Certificate of Facsimile Transmission

I hereby certify that this correspondence is being submitted by facsimile to the Office of Initial Patent Examination's Filing Receipt Corrections with the United States Patent Office at Facsimile No. (703) 746-9195 on this 7<sup>th</sup> day of July, 2004.

*Victoria Linne Poulsen*  
Victoria Linne Poulsen

**Request for Corrected Filing Receipt**

Office of Initial Patent Examination's  
Filing Receipt Corrections  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

Sir:

Applicant requests the Patent Office to make the following corrections to the Official Filing Receipt.

1. The Filing date of this application is March 31, 2004, not April 2, 2004, as indicated on the Filing Receipt. A copy of Applicant's U.S. Express Mail Receipt is provided herein to verify the correct filing date of March 31, 2004.

2. The Domestic Priority data as claimed by applicant of the receipt is incorrectly shown on the Official Filing Receipt, it should read

- —This application claims benefit of
  - 60/459097, filed March 31, 2003;
  - 60/528,104, filed December 8, 2003;
- 1146424-1

- 60/523,880, filed November 20, 2003;
- 60/452,707, filed March 7, 2003;
- 60/482,081, filed June 23, 2003;
- PCT/US03/00394 filed on January 6, 2003
- CIP of 10/338,083, filed on January 6, 2003--

A copy of Applicant's Application Transmittal Sheet and a copy of the first page of the above-referenced Application is enclosed to verify that this information was provided at the time of filing.

Applicant has enclosed a copy of the Official Filing Receipt with the change indicated in red. No fee is believed due for this request. If this belief is in error, the Commissioner is authorized to charge any required fees, or credit any overpayment to Deposit Account No. 50-2319 (Our Order No. 34099/US/2 (463077-267)).

Please direct any calls in connection with this application to the undersigned at (415) 781-1989.

Respectfully submitted,

DORSEY & WHITNEY LLP

Dated: 7/6/04

Four Embarcadero Center  
Suite 3400  
San Francisco, California 94111-4187  
Telephone: (415) 781-1989  
Fax No. (415) 398-3249

By: 

Renee M. Kossiak, Reg. 47,717  
Robin M. Silva, Reg. No. 38,304  
Customer No. 32940

1146424-1



## UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22315-1450  
www.uspto.gov

APPL NO.	FILING OR 371 (c) DATE	ART UNIT	FIL FEE REC'D	ATTY. DOCKET NO	DRAWINGS	TOT CLMS	CLS
10/820,465	<del>04/02/2004</del> 3/31/2004	1646	0.00	34099/US/2 463077-00267	7	25	

Robin M. Silva, Esq.  
Dorsey & Whitney LLP  
Intellectual Property Department  
Four Embarcadero Center, Suite 3400  
San Francisco, CA 94111-4187

CONFIRMATION 10/263

## FILING RECEIPT

\*OC000000013030470\*

Date Mailed: 06/11/2004

Receipt is acknowledged of this regular Patent Application. It will be considered in its order and you will be notified as to the results of the examination. Be sure to provide the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please write to the Office of Initial Patent Examination: Filing Receipt Corrections, facsimile number 703-746-9195. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections (if appropriate).

## Applicant(s)

John Rudolph Desjarlais, Pasadena, CA;  
Eugene Alexander Zhukovsky, West Hollywood, CA;

## Assignment For Published Patent Application

Xencor;

60/459097 March 31, 2003

## Domestic Priority data as claimed by applicant

60/528,104 December 8, 2003

This application claims benefit of 60/523,880 11/20/2003  
and claims benefit of 60/482,081 06/23/2003

60/523,880 November 20, 2003

60/482,081 June 23, 2003

## Foreign Applications

60/452,707 March 7, 2003

PT/US/03/00394 January 8, 2003  
10/338,083

If Required, Foreign Filing License Granted: 06/22/2004

Projected Publication Date: To Be Determined - pending completion of Missing Parts

Non-Publication Request: No

Early Publication Request: No

\*\* SMALL ENTITY \*\*

**Title**

April variants and methods thereof

**Preliminary Class**

514

**LICENSE FOR FOREIGN FILING UNDER**  
**Title 35, United States Code, Section 184**  
**Title 37, Code of Federal Regulations, 5.11 & 5.15**

**GRANTED**

The applicant has been granted a license under 35 U.S.C. 184, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" followed by a date appears on this form. Such licenses are issued in all applications where the conditions for issuance of a license have been met, regardless of whether or not a license may be required as set forth in 37 CFR 5.15. The scope and limitations of this license are set forth in 37 CFR 5.15(a) unless another license has been issued under 37 CFR 5.15(b). The license is subject to revocation upon written notification. The date indicated is the effective date of the license, unless an earlier license of similar scope has been issued under 37 CFR 5.13 or 5.14.

This license is to be retained by the licensee and may be used at any time on or after the effective date of the license unless it is revoked. This license is automatically transferred to any related applications(s) filed under 37 CFR 1.53(d). This license is not retroactive.

The grant of a license does not in any way lessen the responsibility of a licensee for the security of the subject matter as imposed by any Government contract or the provisions of existing laws relating to espionage and national security or the export of technical data. Licensees should apprise themselves of current regulations, especially with respect to certain countries, of other agencies, particularly the Office of Defense Trade Controls, Department of State (with respect to Arms, Munitions and Implements of War (22 CFR 121-128)); the Office of Export Administration, Department of Commerce (15 CFR 370.10 (i)); the Office of Foreign Assets Control, Department of Treasury (31 CFR Parts 500+) and the Department of Energy.

**NOT GRANTED**

No license under 35 U.S.C. 184 has been granted at this time, if the phrase "IF REQUIRED, FOREIGN FILING LICENSE GRANTED" DOES NOT appear on this form. Applicant may still petition for a license under 37 CFR 5.12. If a license is desired before the expiration of 6 months from the filing date of the application. If 6 months has lapsed from the filing date of this application and the licensee has not received any indication of a second order under 35 U.S.C. 181, the licensee may foreign file the application pursuant to 37 CFR 5.15(b).

**Customer Copy**  
Label R-F June 2002

**EXPRESS MAIL**

**UNITED STATES POSTAL SERVICE®**

**Post Office To Addressee**

**ORIGIN (POSTAL USE ONLY)**

PO Zip Code: 94119

Day of Delivery: ☒ Next ☐ Second

Desired Date: 3/31/04

Time in AM: 6:36 PM: 12:00

Weight: 1.636 lbs

Flat Rate Envelope: ☐ Insured: ☒ Signature: ☐ Return Receipt: ☐ Insurance Fee: ☐ Total Postage & Fees: \$1.785

**DELIVERY (POSTAL USE ONLY)**

Delivery Attempt: ☐ No. ☐ Day ☐ AM ☐ PM

Delivery Attempt: ☐ No. ☐ Day ☐ AM ☐ PM

Delivery Attempt: ☐ No. ☐ Day ☐ AM ☐ PM

Delivery Attempt: ☐ No. ☐ Day ☐ AM ☐ PM

**TO: (PLEASE PRINT)**

DORSEY & WHITNEY LLP  
4 EMBARCADERO CTR STE 3400  
SAN FRANCISCO CA 94111-4187

34099/4512 3/31/04 RMS/ULP

463077-00267

**FROM: (PLEASE PRINT)**

PHONE: (415) 781 1969

**TO: (PLEASE PRINT)**

MAIL STOP New Application  
COMMISSIONER FOR TRADEMARKS  
2900 CRYSTAL DR  
ARLINGTON VA 22202-3914

**FOR PICKUP OR TRACKING CALL 1-800-222-1811 WWW.USPS.COM**

**EXPRESS MAIL**

# UTILITY PATENT APPLICATION TRANSMISSION

Our Docket No.:  
34099/US/2 463077-00267

Date: March 26,

First Named Inventor: John R. DesJarlais et al.

Title: APRIL VARIANTS AND METHODS TE

1.0F

This paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 C.F.R. 1. indicated and is addressed to the Mail Stop Patent Application, Commissioner for Patents, P. O. Box 1450, Alexandria, Virginia 22313-1450 on March 26, 2004.

Express Mail No.: EV-424739171 US

Date of Deposit: March 31, 2004

ADDRESS TO:

Box Patent Application  
Commissioner for Patents  
Washington, D.C. 20231

## APPLICATION ELEMENTS

1. ☒ Fee Calculation Sheet  
(Submit an original and a duplicate for fee processing)
2. ☒ Applicant claims small entity status
3. ☒ Specification Total Pages: 54
  - ☒ Descriptive title of the invention
  - ☒ Cross References to Related Applications
  - ☐ Statement Regarding Fed. Sponsored R&D
  - ☐ Reference to Microfiche Appendix
  - ☒ Background of the Invention
  - ☒ Brief Summary of the Invention
  - ☒ Brief Description of the Drawings
  - ☒ Detailed Description
  - ☒ Claims
  - ☒ Abstract of the Disclosure
4. ☒ Drawings (35 U.S.C. 113) Total Sheets: 7
5. ☐ Oath or Declaration Total Pages:
  - a. ☐ Newly Executed (original or copy)
  - b. ☐ Copy from a prior application (37 C.F.R. 1.63(d)) (for continuation/divisional with Box 19 completed)
    1. ☐ DELETION OF INVENTORS  
Signed statement attached deleting inventor(s) named in the prior application (37 C.F.R. 1.63(d)(2) and 1.33(b))
6. ☒ Application Data Sheet (37 C.F.R. 1.76)

7. ☐ CD-ROM or CD-R in duplicate, large table or computer Program (Appendix)
8. ☐ Nucleotide and/or Amino Acid Sequence Submission (If applicable, all necessary)
  - a. ☐ Computer Readable Form (CRF)
  - b. ☐ Specification Sequence Listing on:
    - i. ☐ CD-ROM or CD-R (2 copies); or
    - ii. ☐ Paper
  - c. ☐ Statement verifying identity of above c.

## ACCOMPANYING APPLICATION PAPER

9. ☐ Certification Under 35 U.S.C. 122(b)(2)(B)(i)
10. ☐ Assignment Papers (cover sheet & document(s))
11. ☐ 37 C.F.R. 3.73(b) Submission
12. ☐ Power of Attorney
13. ☐ English Translation Document (if applicable)
14. ☐ Information Disclosure Statement (with Copies of Citations as necessary)
15. ☐ Preliminary Amendment Total Pages:
16. ☒ Return Receipt Postcard (Should be specifically itemized)
17. ☐ Certified Copy of Priority document(s) (if foreign priority is claimed)
18. ☐ Other

19. If a CONTINUING APPLICATION, check appropriate box and supply the requisite information:

☐ Continuation ☐ Division ☒ Continuation-in-part (CIP) of prior Application No.: U.S. Serial No. 60/459097, filed March 31, 2003; 60/528,104, filed December 8, 2003; 60/523,880, filed November 20, 2003; 60/482,081, filed June 23, 2003; 60/452,707, filed March 7, 2003; and USSN 10/338,083 and PCT/US03/00394 filed on January 6, 2003.

## CORRESPONDENCE ADDRESS

ATTY NAME	Robin M. Silva Reg. No. 38,304	SIGNATURE: <i>Robin M. Silva</i>	DATE: March 26, 2004
ADDRESS	DORSEY & WHITNEY LLP Four Embarcadero Center Suite 3400 San Francisco, California 94111-4187		
TELEPHONE	(415) 781-1989		
FAX	(415) 398-3249		
	Customer Number: 32940		



PATENT APPLICATION  
ATTORNEY DOCKET NO.: 34099/US/2 463077-26  
U.S. Express Mail EV- US 424739171 U:

## APRIL VARIANTS AND METHODS THEREOF

[001] This application claims benefit under 35 U.S.C. §199(e) to USSNs 60/459097, filed March 3, 2003; 60/528,104, filed December 8, 2003; 60/523,880, filed November 20, 2003; 60/482,081, filed June 23, 2003; 60/452,707, filed March 7, 2003; and USSN 10/338,083 and PCT/US03/00394 filed on January 6, 2003, all of which are expressly incorporated by reference in their entirety.

### FIELD OF THE INVENTION

[002] The invention relates to novel proteins of APRIL which modulate the signaling of naturally occurring APRIL and/or other TNF super family (TNFSF) proteins with dominant negative antagonist activity, agonist activity, receptor antagonist activity (also known as competitive inhibition activity) and nucleic acids encoding these proteins. The invention further relates to the use of the novel proteins in the treatment of APRIL and/or TNFSF related disorders, such as pathologies of the immune system and oncological conditions.

### BACKGROUND OF THE INVENTION

[003] APRIL (also known as TRDL-1 alpha, TALL-2, TNFSF13) and its closest homologue, BAFF (also known as B-cell Activation Factor, BLyS, TALL-1, THANK, zTNF4 and TNFSF13B) are members of the TNF super family (TNFSF) of proteins. The prototype of the family, Tumor Necrosis Factor Alpha (TNFA), originally discovered for its *in vivo* effect causing tumors to regress, is a key mediator of inflammation. BAFF and APRIL proteins participate in a variety of cellular and intracellular signaling processes and are synthesized as a type 2 membrane protein, and fold into conserved  $\beta$ -pleated sheet structures. It is known that BAFF and APRIL form homotrimers typical of the TNFSF. In addition, BAFF and APRIL also form heterotrimers together.

[004] The receptors for TNFSF members also represent a family of structurally related molecules, including at least 26 receptors and/or receptor decoy molecules. The extracellular domains of members of this family are composed of multiple repeats of a cysteine-rich domain (CRD), a small protein domain containing six conserved cysteines that form three disulfide bonds. The intracellular domains of these receptors are more diverse, although many members of the family contain a death domain that mediates apoptosis and other receptor signaling events. These members are all capable of inducing apoptosis via interaction with one or more intracellular adaptor molecules that also contain death domains. Other signaling receptors of this family signal via interactions with a family of adaptor molecules called TRAFs (TNF receptor associated factors). Signaling through APRIL receptors (for example, TACI and BMCA) is triggered by binding of an oligomeric (and for the most part, trimeric) APRIL ligand.

[005] The three-dimensional structures of BAFF and APRIL are made up of a sandwich of two antiparallel beta-sheets with the "jelly roll" or Greek key topology and it assembles into a trimeric